

The listing of claims will replace all prior versions and listing of claims in the application:

Listing of Claims:

Cell
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Claim 1. (currently amended) A method for inhibiting or reducing the growth of a cell, comprising:
administering a dose of a telomere damage-inducing agent to the cell wherein such agent causes damaged or shortened telomeres within 24 hours or prior to the initiation of the apoptosis cascade, or causes telomere damage followed by a transient increase in telomerase activity; and
administering a dose of telomerase inhibitory agent to the cell, such that an inhibition or reduction in the growth of the cell is achieved.

Claim 2. (currently amended) A method for improving the efficacy of a telomere damage-inducing agent, in a subject, comprising:
administering a dose of a telomere damage-inducing agent to the cell wherein such agent causes damaged or shortened telomeres within 24 hours or prior to the initiation of the apoptosis cascade, or causes telomere damage followed by a transient increase in telomerase activity; and
administering a dose of telomerase inhibitory agent to the cell, such that the telomerase inhibitory agent enhances the efficacy of the telomere damage-inducing agent, relative to the effect of the telomere damage-inducing agent in the absence of the telomerase inhibitory agent.

Claim 3. (Original) The method of any one of claims 1 or 2, wherein said growth is aberrant.

Claim 4. (Original) The method of any one of claims 1 or 2, wherein said cell is a tumor cell.

Claim 5. (Original) The method of any one of claims 1 or 2, wherein said cell is a leukemia cell.

Claim 6. (Original) The method of claim 4, wherein said tumor cell is of the brain, breast, ovary, testes, bladder, prostate, colon, lung, liver, pancreas, or uterus.

Claim 7. (Original) The method of claim 4, wherein said tumor cell is benign.

Claim 8. (Original) The method of claim 4, wherein said tumor cell is malignant.

Claim 9. (Original) The method of any one of claims 1 or 2, wherein said growth is selected from the group consisting of hyperplastic and hypertrophic.

Claim 10. (Original) The method of any one of claims 1 or 2, wherein said inhibition or reduction in the growth of the cell comprises apoptosis.

Claim 11. (Original) The method of any one of claims 1 or 2, wherein said telomere damage-inducing agent and telomerase inhibitory agent are administered serially.

Claim 12. (Original) The method of any one of claims 1 or 2, wherein said telomere damage-inducing agent and telomerase inhibitory agent are administered concurrently.

Claim 13. (Original) The method of any one of claims 1 or 2, wherein said telomere damage-inducing agent and telomerase inhibitory agent are administered in any order.

Claim 14. (Original) The method of any one of claims 1 or 2, wherein said telomere damage-inducing agent or telomerase inhibitory agent, is administered as a timed-release formulation.

Claim 15. (Original) The method of claim 14, wherein said telomere damage-inducing agent and telomerase inhibitory agent are both administered as a timed-release formulation.

Claim 16. (Original) The method of any one of claims 1 or 2, wherein said telomere damage-inducing agent or telomerase inhibitory agent, is administered locally.

Claim 17. (Original) The method of claim 16, wherein said telomere damage-inducing agent and telomerase inhibitory agent are both administered locally.

Claim 18. (Original) The method of any one of claims 1 or 2, wherein said telomere damage-inducing agent or telomerase inhibitory agent, is administered systemically.

Claim 19. (Original) The method of claim 18, wherein said telomere damage-inducing agent and telomerase inhibitory agent are both administered systemically.

Claim 20. (Original) The method of any one of claims 1 or 2, wherein said telomere damage-inducing agent or telomerase inhibitory agent, is administered regionally.

Claim 21. (Original) The method of claim 20, wherein said telomere damage-inducing agent and telomerase inhibitory agent are both administered systemically.

Claim 22. (Original) The method of any one of claims 1 or 2, wherein said cell is in a human.

Claim 23. (Original) The method of any one of claims 1 or 2, wherein said telomere damage-inducing agent is paclitaxel, or a derivative thereof.

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Claim 24. (currently amended) The method of any one of claims 1 or 2, wherein said telomerase inhibitory agent is a nucleoside analog, or derivative thereof.

Claim 25. (withdrawn) The method of any one of claims 1 or 2, wherein said telomerase inhibitory agent is an antisense nucleic acid corresponding to a telomerase

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Claim 26. (currently amended) The method of claim 24, wherein said nucleoside analog is AZT in a dose of no more than about 0.24 mg/kg/day.

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Claim 27. (currently amended) The method of claim 24, wherein said nucleoside analog is d4T in a concentration of at least about 20 micromolar.

Claim 28. (Original) The method of any one of claims 1 or 2, wherein said agent selected from the group consisting of telomere damage-inducing agent and telomerase inhibitory agent, is administered as a subtherapeutic dose.

Claim 29 (withdrawn). A method of identifying an agent that inhibits or reduces the growth of a cell by inducing telomere damage in said cell comprising,
contacting a cell with an agent; and

determining if telomere damage has occurred to identify thereby an agent that inhibits or reduces growth of a cell.

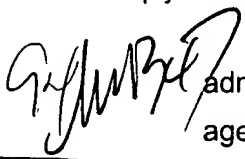
Claim30 (withdrawn). A method of identifying an agent or agents that inhibits or reduces the growth of a cell comprising,
contacting a cell with at least one agent and determining if telomere damage has occurred; and
contacting a cell with the same or at least one other agent and determining if a reduction in telomerase activity has occurred, whereby an agent or agents, alone or in combination, that are determined to induce telomere damage and inhibit telomerase activity, are indicated as an agent or agents that inhibits or reduces the growth of a cell.

Claim 31 (withdrawn). An agent or agents identified according to the method of claim 30.

Claim 32 (withdrawn). A pharmaceutical composition comprising an agent or agents identified according to the method of claim 30, and a pharmaceutically acceptable carrier.

Claim33 (currently amended). A method of inhibiting or reducing the growth of a cell comprising:
contacting a cell with at least one agent and determining if telomere damage has occurred;
contacting a cell with the same or at least one other agent and determining if a reduction in telomerase activity has occurred, whereby an agent or agents, alone or in combination, that are determined to induce telomere damage and inhibit telomerase activity, are indicated as an agent or agents that inhibits or reduces the growth of a cell; and
administering to a cell a therapeutically effective amount of the identified agent or agents.

Claim34 (currently amended). A method of treating aberrant cell growth in a mammal comprising:
contacting a cell with at least one agent and determining if telomere damage has occurred;
contacting a cell with the same or at least one other agent and determining if a reduction in telomerase activity has occurred, whereby an agent or agents, alone or in combination, that are determined to induce telomere damage and inhibit telomerase activity, are indicated as an agent or agents that inhibits or reduces the growth of a cell; and

 administering to a mammal a therapeutically effective amount of the identified agent or agents.

Claim 35 (original). The method of claim 34 wherein said mammal is a human.


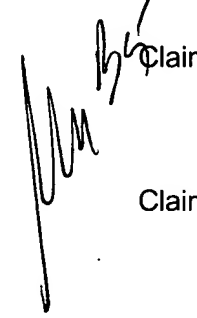
Claim 36 (withdrawn). A composition suitable for inhibiting or reducing the growth of a cell comprising,
a therapeutically effective amount of telomere damage-inducing agent; and
a therapeutically effective amount of telomerase inhibitory agent.

Claim 37 (withdrawn). An article of manufacture comprising,
a vial containing a purified telomere damage-inducing agent and a purified telomerase inhibitory agent; and
instructions for use.

Claim 38 (withdrawn). The article of claim 37, wherein said purified telomere damage-inducing agent and purified telomerase inhibitory agent are packaged in separate vials.

Claim 39 (withdrawn). The method of claim 37, wherein said purified telomere damage-inducing agent and purified telomerase inhibitory agent are formulated in a pharmaceutically-acceptable carrier.

Claim 40. (currently amended) A method of treating cancer in a patient comprising,
administering a therapeutically-effective amount of a telomere damage-inducing agent to said patient wherein such agent causes damaged or shortened telomeres within 24 hours or prior to the initiation of the apoptosis cascade, or causes telomere damage followed by a transient increase in telomerase activity; and
administering a therapeutically-effective amount of a telomerase inhibitory agent to said patient, such that treatment of the cancer is achieved.


 Claim 41 (currently amended). The method of claim 40, wherein the method further comprises identifying a patient having cancer.

Claim 42. (currently amended) A method of treating cancer in a patient comprising,

obtaining an agent selected from the group consisting of a telomere damage-inducing agent wherein such agent causes damaged or shortened telomeres within 24 hours or prior to the initiation of the apoptosis cascade, or causes telomere damage followed by a transient increase in telomerase activity, and a telomerase inhibitory agent;
administering a therapeutically-effective amount of said telomere damage-inducing agent to said patient; and
administering a therapeutically-effective amount of a telomerase inhibitory agent to said patient, such that treatment of the cancer is achieved.

Claim 43 (currently amended). The method of claim 42, wherein the method further comprises identifying a patient having cancer.

Claim 44 (original). The method of any one of claims 40 or 42, wherein said telomere damage-inducing agent is paclitaxel, or a derivative thereof.

Claim 45 (currently amended). The method of any one of claims 40 or 42, wherein said telomerase inhibitory agent is a nucleoside analog, or derivative thereof.

Claim 46 (currently amended). The method of claim 45, wherein said nucleoside analog is AZT.

Claim 47 (currently amended). The method of claim 45, wherein said nucleoside analog is d4T.

Claim 48 (withdrawn). The method of any one of claims 40 or 42, wherein said telomerase inhibitory agent is an antisense nucleic acid corresponding to a telomerase.

Claim 49 (withdrawn). A method of enhancing the efficacy of a chemotherapeutic agent comprising,
administering a chemotherapeutic agent to a cell in the presence of a telomerase inhibitory agent, whereby the efficacy of the chemotherapeutic agent is increased as compared to a control.

Claim 50 (withdrawn). A method of reducing or inhibiting the resistance of a cell to an anticancer agent comprising,

administering an anticancer agent to a cell in the presence of a telomerase inhibitory agent, whereby the resistance of said cell to said anticancer agent is decreased as compared to a control.

Claim 51 (withdrawn). The method of claims 49 or 50, wherein said anticancer agent is a telomere damage-inducing agent.

Claim 52 (withdrawn). The method of claim 51, wherein said telomere damage-inducing agent is paclitaxel.

Claim 53 (withdrawn). The method of claims 49 or 50, wherein said telomerase inhibitory agent is a nucleotide analog or derivative thereof.

Claim 54 (withdrawn). The method of claim 53, wherein said nucleotide analog is AZT.

Claim 55 (withdrawn). The method of claim 53, wherein said nucleotide analog is d4T.

Claim 56 (withdrawn). The method of claims 49 or 50, wherein said telomerase inhibitory agent is an antisense nucleic acid corresponding to a telomerase.

Claim 57 (withdrawn). A method for detecting telomerase activity in cell extract comprising:
incubating a reaction mixture comprising a cell extract, a nucleic acid substrate for a telomerase, and nucleotide triphosphates for a time sufficient for the nucleic acid substrate to be polymerized;
contacting the substrate with at least one nucleic acid primer and subjecting the substrate to a polymerase chain reaction; and
detecting the presence of polymerase chain reaction products to detect thereby telomerase activity in said cell extract.

Claim 58 (withdrawn). The method of claim 57, wherein the cell extract is derived from a cell that has been contacted with an agent.

Claim 59 (withdrawn). The method of claim 57, wherein the method further comprises contacting the cell extract with an agent.

Claim 60 (withdrawn). The method of claim 57, wherein the agent is a telomerase inhibitory agent.

Claim 61 (withdrawn). The method of claim 60, wherein the telomerase inhibitory agent is AZT.

Claim 62 (withdrawn). The method of claim 60, wherein the telomerase inhibitory agent is d4T.

Claim 63 (withdrawn). The method of claim 57, wherein the telomerase inhibitory agent is an antisense nucleic acid corresponding to a telomerase.

Claim 64 (withdrawn). The method of claim 57, wherein the cell extract is derived from a human cell.

Claim 65 (withdrawn). The method of claim 59, wherein the nucleic acid substrate comprises the sequence provided in SEQ ID NO: 10.

Claim 66 (withdrawn). The method of claim 59, wherein the nucleic acid primer comprises the sequence provided in SEQ ID NOS: 1 and 2.

Claim 67 (withdrawn). The method of claim 59 wherein the nucleic acid primer is labeled with a radioisotope.

Claim 68 (withdrawn). The method of claim 59 wherein said nucleic acid primer is labeled with a fluorescent label.

Claim 69 (withdrawn). A method for determining telomere length comprising:
hybridizing telomeric DNA fragments with a telomere probe; and
determining the amount of hybridized telomere probe present, whereby the amount of hybridized telomere probe present is an indication of telomere length.

Claim 70 (withdrawn). The method of claim 69, wherein the telomeric DNA fragments are produced using a restriction enzyme.

Claim 71 (withdrawn). The method of claim 70, wherein the restriction enzyme or enzymes is selected from the group consisting of *HinfI*, *HaeIII*, and *HhaI*.

Claim 72 (withdrawn). The method of claim 69, wherein the telomeric DNA is derived from a cell.

Claim 73 (withdrawn). The method of claim 69, wherein the cell has been contacted with an agent.

Claim 74 (withdrawn). The method of claim 73, wherein the agent is a telomerase inhibitory agent.

Claim 75 (withdrawn). The method of claim 74, wherein the telomerase inhibitory agent is AZT.

Claim 76 (withdrawn). The method of claim 74, wherein the telomerase inhibitory agent is d4T.

Claim 77 (withdrawn). The method of claim 74, wherein the telomerase inhibitory agent is an antisense nucleic acid corresponding to a telomerase.

Claim 78 (withdrawn). The method of claim 72, wherein the cell is from a human.

Claim 79 (withdrawn). The method of claim 69, wherein the telomere probe comprises the sequence provided in SEQ ID NO: 10.

Claim 80 (withdrawn). The method of claim 69, wherein the telomere probe comprises the sequence provided in SEQ ID NO: 11.

Claim 81 (withdrawn). The method of claim 69, wherein the telomere probe is labeled with a radioisotope.

Claim 82 (withdrawn). The method of claim 69, wherein the telomere probe is labeled with a fluorescent label.

Claim 83 (withdrawn). The method of claim 1, wherein said telomere damage inducing agent is formulated as a nanoparticle comprising a cross linked gelatin.

Claim 84 (withdrawn). The method of claim 1, wherein said telomerase inhibitory agent is formulated as a nanoparticle comprising a cross-linked gelatin.

Claim 85 (withdrawn). The method of any one of claims 83 or 84, wherein said nanoparticle is about 500 nm to about 1 μ m in diameter.

Claim 86 (withdrawn). The method of claim 1, wherein said telomere damage inducing agent is formulated as a microparticle.

Claim 87 (withdrawn). The method of claim 1, wherein said telomerase inhibitory agent is formulated as a microparticle.

Claim 88 (withdrawn). The method of any one of claims 86 or 87, wherein said microparticle is about 1 μ m to about 10 μ m in diameter.

Claim 89 (withdrawn). A method of identifying a telomerase inhibitory agent comprising:
contacting a cell with an agent;
incubating a reaction mixture comprising an extract of said cell, a nucleic acid substrate for a telomerase, and nucleotide triphosphates for a time sufficient for the nucleic acid substrate to be polymerized;
contacting the substrate with at least one nucleic acid primer and subjecting the substrate to a polymerase chain reaction; and
detecting a decrease in the presence of polymerase chain reaction products to thereby identify a telomerase inhibitory agent.

Claim 90 (new). The method of claim 24, wherein said nucleoside analog is d4T in a dose that produces at least about 20 micromolar plasma concentration in a subject.

Claim 91 (new). The method of any one of claims 26, wherein said telomere damage-inducing agent is paclitaxel, or a derivative thereof, and the ratio of the AZT concentration to the telomere damage-inducing agent concentration is about 40:60 of their respective therapeutic concentrations.

Claim 92 (new). The method of any one of claims 26, wherein said telomere damage-inducing agent is paclitaxel, or a derivative thereof, and the ratio of the AZT concentration to the telomere damage-inducing agent concentration is about 40:60 of their respective therapeutic doses.